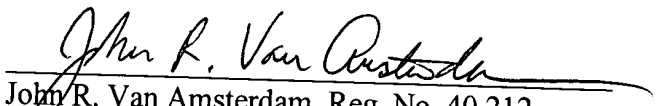
residues, but this peptide proved incapable of sensitizing EBV-B cells to lysis by CTL 41. In contrast, peptides MEVDPIGHLY (SEQ ID NO:59) and EVDPIGHLY (SEQ ID NO:56) scored positive in this cytotoxicity assay and produced half-maximal lysis of autologous EBV-B target cells at ~0.05 nM (Fig. 11). This half-maximal lysis peptide concentration is lower than with the other MAGE antigenic peptides which produce half-maximal lysis at peptide concentrations from ~0.1 to ~25 nM (Chaux et al., *J. Immunol.* 163:2928, 1999; Traversari et al., *J. Exp. Med.* 176:1453, 1992; van der Bruggen et al., *Eur. J. Immunol.* 24:2134, 1994; Luiten and van der Bruggen, *Tissue Antigens* 55:149, 2000). Thus, the epitope recognized by CTL 41 does not contain consensus anchor residues for HLA-B35. It would therefore not have been discovered by an approach based on candidate peptides chosen on the basis of their sequence and used for *in vitro* stimulation of T lymphocytes. Peptides MEVDPIGHLY (SEQ ID NO:59) and EVDPIGHLY (SEQ ID NO:56) are encoded by the MAGE-A3 gene but not by another MAGE gene.

Remarks

During the preparation of a response to the Examiner's requirement for information under 37 C.F.R. 1.105, Applicants observed that the amino acid sequence of a MAGE-A3 peptide described in the application (SEQ ID NO:57), did not match the sequence of the portion of the MAGE-A3 protein from which it was derived. SEQ ID NO:57 was described as corresponding to MAGE-$A3_{167-182}$. The sequence of the peptide was reported as MEVDPIGHLYIFACTL, while the correct sequence of this portion of the MAGE-A3 protein, as provided in SEQ ID NO:55 is: MEVDPIGHLYIFATCL. Applicants have amended the specification and submitted a revised Sequence Listing to correct this typographical error.

If the Examiner has any question concerning the foregoing amendment, the Examiner is invited to telephone the undersigned at the number listed below.

Respectfully submitted,



John R. Van Amsterdam, Reg. No. 40,212
WOLF, GREENFIELD & SACKS, P.C.
600 Atlantic Avenue
Boston, Massachusetts 02210
Tel: (617) 720-3500

Attorney's Docket No. L00461/70104
Dated: August 9, 2002
XNDD

Amended Paragraph

Peptide [MEVDPIGHLYIFACTL] MEVDPIGHLYIFATCL (MAGE-A3$_{167-182}$; SEQ ID NO:57) scored positive. The consensus anchor residues for HLA-B35 are P in position 2 and Y, F, M, L or I in position 9 (Rammensee, H.G., J. Bachmann, and S. Stevanovic. 1997. *MHC Ligands and Peptide Motifs*. Springer, New York). Peptide DPIGHLYIF (SEQ ID NO:58) contained the consensus anchor residues, but this peptide proved incapable of sensitizing EBV-B cells to lysis by CTL 41. In contrast, peptides MEVDPIGHLY (SEQ ID NO:59) and EVDPIGHLY (SEQ ID NO:56) scored positive in this cytotoxicity assay and produced half-maximal lysis of autologous EBV-B target cells at ~0.05 nM (Fig. 11). This half-maximal lysis peptide concentration is lower than with the other MAGE antigenic peptides which produce half-maximal lysis at peptide concentrations from ~0.1 to ~25 nM (Chaux et al., *J. Immunol.* 163:2928, 1999; Traversari et al., *J. Exp. Med.* 176:1453, 1992; van der Bruggen et al., *Eur. J. Immunol.* 24:2134, 1994; Luiten and van der Bruggen, *Tissue Antigens* 55:149, 2000). Thus, the epitope recognized by CTL 41 does not contain consensus anchor residues for HLA-B35. It would therefore not have been discovered by an approach based on candidate peptides chosen on the basis of their sequence and used for *in vitro* stimulation of T lymphocytes. Peptides MEVDPIGHLY (SEQ ID NO:59) and EVDPIGHLY (SEQ ID NO:56) are encoded by the MAGE-A3 gene but not by another MAGE gene.

Alignment of peptides with MAGE-A1/SEQ ID NO:2 (residues 145-172 shown)

```
Gly Lys Ala Ser Glu Ser Leu Gln Leu Val Phe Gly Ile Asp Val Lys Glu Ala Asp Pro Thr Gly His Ser Tyr Val Leu Val (SEQ 2)
145                 150                 155                 160                 165                 169

                                                        Glu Ala Asp Pro Thr Gly His Ser Tyr Val Leu Val (SEQ 5)
                                                            Asp Pro Thr Gly His Ser Tyr Val Leu Val (SEQ 6)
                                                            Asp Pro Thr Gly His Ser Tyr Val Leu     (SEQ 7)
                                                        Glu Ala Asp Pro Thr Gly His Ser Tyr         (SEQ 8)
                                                    Lys Glu Ala Asp Pro Thr Gly His Ser Tyr         (SEQ 9)
        Met Ser Glu Ser Leu Gln Leu Val Phe Gly Ile Asp Val Lys Glu Ala Asp Pro Thr Gly His Ser Tyr (SEQ 10)
                                                    Met Glu Ala Asp Pro Thr Gly His Ser Tyr         (SEQ 12)
                                                        Met Ala Asp Pro Thr Gly His Ser Tyr         (SEQ 14)
                                                    Xaa Glu Ala Asp Pro Thr Gly His Ser Tyr         (SEQ 53)
```

SEQ ID NO:5 aligns with residues 161-172 of SEQ ID NO:2
SEQ ID NO:6 aligns with residues 163-172 of SEQ ID NO:2
SEQ ID NO:7 aligns with residues 163-171 of SEQ ID NO:2
SEQ ID NO:8 aligns with residues 161-169 of SEQ ID NO:2
SEQ ID NO:9 aligns with residues 160-169 of SEQ ID NO:2
SEQ ID NO:10 aligns with residues 162-169 of SEQ ID NO:2
SEQ ID NO:12 aligns with residues 148-169 of SEQ ID NO:2
SEQ ID NO:14 aligns with residues 161-169 of SEQ ID NO:2
SEQ ID NO:16 aligns with residues 162-169 of SEQ ID NO:2
SEQ ID NO:53 aligns with residues 161-169 of SEQ ID NO:2

Alignment of peptides with MAGE-A3/SEQ ID NO55 (residues 163-185 shown)

```
Gly Ile Glu Leu Met Glu Val Asp Pro Ile Gly His Leu Tyr Ile Phe Ala Thr Cys Leu Gly Leu Ser (SEQ ID NO:55)
       165                 170                 175                 180                 185

            Glu Val Asp Pro Ile Gly His Leu Tyr                                                (SEQ ID NO:56)
          Met Glu Val Asp Pro Ile Gly His Leu Tyr Ile Phe Ala Thr Cys Leu                      (SEQ ID NO:57)
                   Asp Pro Ile Gly His Leu Tyr Ile Phe                                         (SEQ ID NO:58)
          Met Glu Val Asp Pro Ile Gly His Leu Tyr                                              (SEQ ID NO:59)
```

SEQ ID NO:56 aligns with residues 168-176 of SEQ ID NO:55
SEQ ID NO:57 aligns with residues 167-182 of SEQ ID NO:55
SEQ ID NO:58 aligns with residues 170-178 of SEQ ID NO:55
SEQ ID NO:59 aligns with residues 167-176 of SEQ ID NO:55